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PATRICIA GRANAHAN
HAMILTON BROOK SMITH & REYNOLDS
TWO MILITIA DRIVE
LEXINGTON MA 02173-4799

EXAMINER

SHUKLA, R

ART UNIT

PAPER NUMBER

1632

DATE MAILED:

08/31/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

8-31-99

Office Action SummaryApplication No.
08/984,178

Applicant(s)

Horvitz et al

Examiner

Ram Shukla

Group Art Unit

1632

- ☐ Responsive to communication(s) filed on _____.
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 1-68 is/are pending in the application.

Of the above, claim(s) 5-7, 16, 19, 20, 23, 24, 28-32, 34, 37-39, and 41-68 are withdrawn from consideration.

- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 1-4, 8-15, 17, 18, 21, 22, 25-27, 33, 35, 36, and 40 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claims _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☒ Notice of References Cited, PTO-892
- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 11
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

1. Amendment filed 6-17-99 (Paper No 10), electing the invention of group I, claims 1-4, 8-15, 17, 18, 21, 22, 25-27, 33, 35, 36, and 40 is entered.
2. Claims 5-7, 16, 19, 20, 23-24, 28-32, 34, 37-39 and 41-68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention. Election was made **without** traverse in Paper No. 10.
3. Instant application is a continuation of 08/287669 which is a divisional of 07/979638 which is a continuation-in-part of 7/897,788.

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

First page of the specification does not contain reference to parent application 07/979,638, that is now abandoned. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1- 4, 8-15, 17, 18, 22, 33, 35, and 40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for: ced-3 gene disclosed in Seq ID No 18 or the DNA encoding the amino acid sequence of Seq ID No 19; ced-3 mutants listed in table-3 (see page 62 of the specification); and ced-4 mutants listed in table-2 (see page 61 of the specification); and probes and primers designed on the basis of these sequences, does not reasonably provide enablement for, isolated DNAs for any and all ced-3 genes, the RNA encoded thereof, isolated DNAs for any and all ced-3 or ced-4 genes or probes thereof. The specification

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does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 recites an isolated DNA which is the ced-3 gene, whereas claim 2 recites an isolated DNA disclosed in the Seq ID No 18. Claim 3 is drawn to the nucleotide sequence that encodes the amino acid sequence disclosed in Seq ID No 19. Claim 4 recites the isolated RNA encoded by the DNA of claim 1. The invention of claims 8-15, 17, 18, 21, 22, 33, 35, and 40 has been summarized previously in para 6 above.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided.

The specification is not enabling for the claimed invention because the specification does not provide sufficient guidance as to how an artisan would have made all the isolated DNAs for the ced-3 genes, mutants of ced-3 and ced-4 genes and the probes from all these DNAs claimed above and would have used these without undue experimentation.

As discussed in para 6 above, the instantly presented invention as claimed encompasses DNAs of: any and all ced -3 genes, mutants of ced-3 and ced-4 genes, genes that are structurally and functionally related to ced-3 or ced-4 genes, from any and all organisms including microbes, invertebrates, vertebrates and plants (see pages 2 and 3 of specification).

However, the specification does not provide how would an artisan have made all these innumerable DNAs from all the living organisms? Even if one had to assume that using various screening and other molecular biology techniques described in the specification and available in prior art, an artisan would have been able to make these DNAs, would all the polypeptides encoded by the isolated DNAs would have any specific functions? For example, what would have been the function of every possible mutant of ced-3 or ced-4 gene? Further, would all the living organisms have ced-3 or ced-4 genes or even if they do have, would the proteins encoded

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by these genes be same in all the organisms or would they have same function or would require similar cofactor? In the absence of any function, what would have been the use of making all these DNAs, probes from these DNAs or use these probes for isolating more DNAs or developing bioassays for isolating other DNAs? Furthermore, as discussed in para 6, just because the claimed DNAs or encoded polypeptides may have some sequence similarity or functional similarity (although, the extent of sequence or functional similarity is not disclosed in the specifications), does not ensure that the resultant DNAs, their encoded polypeptides or mutants thereof would have the same function or even any function as that of the said known protein. Moreover, amplification of sequences using PCR under different reaction conditions can produce numerous DNA sequences. There will be no way of knowing what sequences will be obtained by these methods and what would have their function or use been, if any. The specification does not provide any guidance as to how an artisan would have determined what would have been the function of all these polynucleotides and how would these multitude of polynucleotide would have been used or for what use.

It is concluded that the specification as filed is not enabling for the claimed invention as filed and an artisan would not have been able to practice the invention without undue experimentation. Therefore, limitation of the scope of the invention to an *ced-3* gene disclosed in Seq ID No 18 or the DNA encoding the amino acid sequence of Seq ID No 19; *ced-3* mutants listed in table-3 (see page 62 of the specification); and *ced-4* mutants listed in table-2 (see page 61 of the specification); and probes and primers designed on the basis of these sequences, is proper.

7. Claims 1, 4, 8, 15, 17, 18, 22, 33, 35, 36, and 40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is referred to the interim guidelines on written description published June 15, 1998 in the Federal Register at Volume 63, Number 114, pp 32639-32645 (also available at www.uspto.gov).

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The invention of claims 1, 4, 8, 15, 17, 18, 22, 33, 35, 36, and 40 has been summarized previously in para 6 above.

As discussed in para 6 above, the instantly presented invention as claimed encompasses DNAs of: any and all ced -3 genes, mutants of ced-3 and ced-4 genes, genes that are structurally and functionally related to ced-3 or ced-4 genes, from any and all organisms including microbes, invertebrates, vertebrates and plants (see pages 2 and 3 of specification). However, the specification discloses only Seq ID No 18 that encodes a polypeptide disclosed in Seq ID No 19 and certain mutants of ced-3 and ced-4 gene disclosed in tables 2 and 3. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, specification discloses ced-3 and ced 4 genes that have the Sequence of ID No 19 and Seq ID No 1 and mutants that have mutations in single nucleotides. There is no indication what other nucleotides would have been mutated, for example, in bioassays. Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence). In the instant case, the only other identifying characteristics is that these are structurally and functionally related and that they may have sequence similarity in a calcium-binding, however, no disclosure about the extent or type of sequence or functional relationship has been provided. This limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant was in possession of DNAs besides Seq ID No 18 that encodes a polypeptide disclosed in Seq ID No 19 and certain mutants of ced-3 and ced-4 gene disclosed in tables 2 and 3, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 1-4, 8-15, 17, 18, 21, 22, 25, 33, 35, 36, and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4, 8-15, 17, 18, 21, 22, 25, 33, 35, 36, and 40 are indefinite because these claims define the claimed nucleic acids by a name only. Reference of a nucleic acid by name is indefinite and unclear because any other nucleic acid can be given a certain name irrespective of its function and structure. To clearly identify a certain nucleic acid, it should be characterized by its sequence, protein made, functional activity and characteristics of the protein. Claims 8-15 are also indefinite because they recite "the activity of the gene". However, it is not unclear what is encompassed by the "activity of the gene"?

Claims 17, 18, 21, and 22 are indefinite because they recite the phrase "structurally related" and "functionally related", however these phrases are not clearly defined in the specification. For example, in relation to structurally related in terms of sequence, what is the degree of relatedness. Likewise, what functions and to what degree a given gene is related to claimed gene.

Claim 10 is indefinite because it defines mutations by the amino acid, not by nucleotides sequence. Recitation of the mutation in the DNA and the resultant amino acid change will be appropriate.

Claims 21 and 22 are indefinite because they are not limited to nucleic acid, and so do not reflect applicant's election of nucleic acids.

Claims 25, 33, 35, 36, and 40 are indefinite because they are dependent on non-elected claims.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 8, 15, 17, 18, 22, 35, 36, and 40 rejected under 35 U.S.C. 102(b) as being anticipated by Yuan (1990).

The invention of claims 8, 15, 17, 18, 22, 35, 36, and 40 has been previously described in para 6.

Yuan teaches the DNA and transcript for ced-4 gene and its mutant n1416 (see the abstract on page 125 and description of n1416 plasmid and used of n1416 plasmid to identify ced-4 gene on page 131, 133 and 137). The n1416 mutant is produced due to the insertion of Tc4 transposon in the ced-4 gene and produces transcription products that have different sizes compared to the wild type ced-4 gene. Yuan also teaches that ced-4 gene is related to ced-3 gene and therefore can be used for making probes. Yuan also teaches bioassay to isolated ced-3 and ced-4 genes. The ced-4 DNA was identified by injecting a cosmid clone containing fragments of *C. elegans* genomic library into oocytes to produce animals expressing target DNA fragments and by comparing the phenotype of the animals with another animals that did not express the said DNA. Expression of n1416 DNA results in the animals that have less dead cells in their head (see page 132).

Therefore, claims 8, 15, 17, 18, 22, 35, 36, and 40 are anticipated by Yuan.

12. Claims 17 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Sumrada et al 1984 (Genbank accession no U43503, J. Bacteriology 160: 1078-1087, 1984).

The invention of claims 17 and 18 has been previously described in para 6.

Sumrada et al teach the nucleotide sequence for the *Saccharomyces arginase* gene (see the sequence comparison). The nucleotide sequence disclosed by Sumrada et al has a 100%

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best local similarity with the Seq ID No 18 (ced-3 gene DNA) in a region of 19 nucleotides. Since the term structural similarity is not clearly defined in the specification, it is interpreted as any sequence similarity over any number of nucleotide sequences.

Therefore, the invention of claims 17 and 18 are anticipated by Sumrada et al.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 26 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yuan et al 1990.

Claims 26 and 27 are directed to methods of identifying ced-3 or ced-4 related gene by, combining primers comprising, parts of a cell death gene or degenerate oligonucleotides derived from the amino acid sequence encoded by the cell death gene, with a nucleic acid, carry out PCR and detect specific DNAs.

Yuan teaches the sequence for ced-4 cell death gene in *C. elegans*. Yuan also teaches that an understanding of how genes cause cells to die, as well as of how genes specify which cells are to live and which cells are to die, is essential for an understanding of animal development (see page 126). Yuan does not teach the identification of ced-3 and ced-4 related genes by PCR using primers based on ced-4 sequences.

At the time of the invention, it would have been obvious to one of ordinary skill in the art to have designed primers based on the DNA sequence of ced-4 gene disclosed by Yuan or based on the amino acid sequence obtained after translating the sequence described by Yuan and carry out PCR using *C. elegans* genomic library as the nucleic acid source with reasonable expectation of success because Yuan teaches the genomic library as well as the sequence for

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ced-3 genes while designing a PCR primer and PCR reactions are routine techniques used in any molecular biology laboratory. An artisan would have been motivated to design primers and carry out the PCR reactions to identify cell death genes because Yuan teaches that understanding of mechanism of action of genes that cause cells to die or live is essential for understanding animal development.

15. No claim is allowed.

16. Claims 1-4, 9-14, 25 and 33 are free of prior art. The references by Yuan et al (Yuan J et al Cell 75:641-652, 1993) and Wilson et al (Wilson R et al Nature 368:32-38, 1994) are made of record because they teach ced-3 gene and the nucleotide sequences of C. elegans chromosome III respectively.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Stanton, can be reached on (703) 308-2801. The fax phone number for this Group is (703) 308-8724.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 305-0196.

Ram R. Shukla, Ph.D.



BRUCE R. CAMPBELL
PRIMARY EXAMINER
GROUP 1800